

L35 ANSWER 209 OF 272 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1991:7266 HCAPLUS Full-text
 DOCUMENT NUMBER: 114:7266
 TITLE: Immunosuppressive fluorinated cyclosporin analogs.
 INVENTOR(S): Durette, Philippe L.; Pessolano, Arsenio A.;
 Kollonitsch, Janos; Witzel, Bruce E.
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA
 SOURCE: Brit. UK Pat. Appl., 56 pp.
 CODEN: BAXXDU
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| GB 2227244 | A1 | 19900725 | GB 1990-1212 | 19900118 |
| US 5227467 | A | 19930713 | US 1991-693783 | 19910429 |
| PRIORITY APPLN. INFO.: | | | US 1989-298712 | A 19890119 |
| | | | US 1987-81255 | B2 19870803 |

OTHER SOURCE(S): MARPAT 114:7266
 GI

x9-x10-x11-x1-x2-x3
 *8-x7-x6-x5_____x4 I

AB The title compds. [I; X1 = NR2C[CH(OH)CHR1CH2XR]CO; X2 = (fluorinated) Abu, Ala, Nva, Ser, Thr, Val; X3 = Sar, D-MeAla; X4, X6, X9, X10 = (fluorinated) MeLeu, MeVal; X5 = (fluorinated) Val, Nva; X7 = (fluorinated) Aba, Abu, Phe; X8 = D-Ala; X11 = (fluorinated) MeVal, MeNva; X = S, SO, SO2, O, NH; R = H, alkyl, alkenyl, thioalkyl, (substituted) pyridyl, Ph, furyl, pyrrolyl, thienyl, etc.; R1 = alkyl; R2 = alkyl,

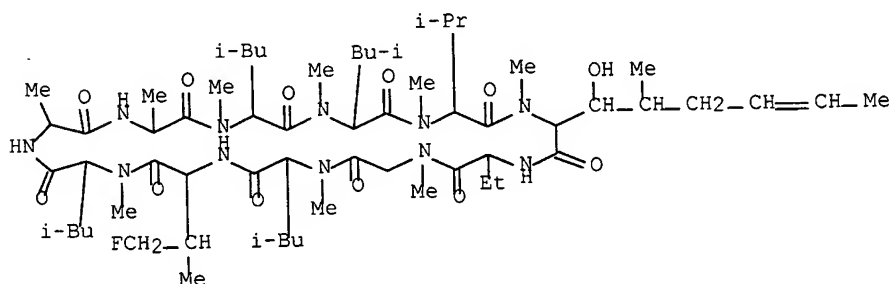
alkylphenyl], were prepared Thus, cyclo[[[(2S, 3R, 4R, 6E)-3-hydroxy-4-methyl-2-methylamino-6-octenoyl]-L-2-aminobutyryl-sarcosyl-N-methyl-L-leucyl-4-fluorovalyl-N-methyl-L-leucyl-L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valine] was prepared by the solution phase method using N,N-bis(2-oxo-3-oxazolidinyl)phosphorodiamidic chloride as a coupling agent. I had 10-163% of the T-cell proliferation inhibitory activity of cyclosporin A.

IT 121893-00-3P 130840-76-5P 130840-77-6P
130840-78-7P 130840-79-8P 130840-80-1P
130840-81-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as immunosuppressant)

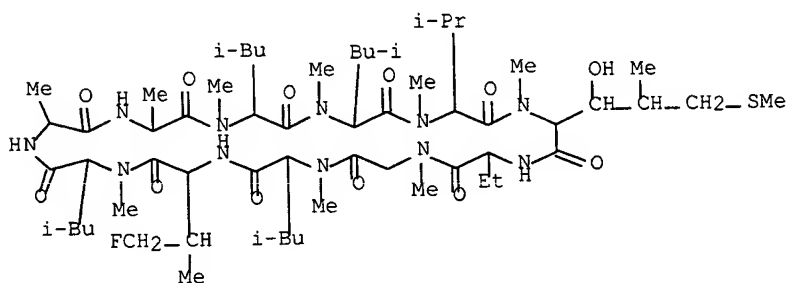
RN 121893-00-3 HCAPLUS

CN Cyclosporin A, 10-(4-fluoro-L-valine)- (9CI) (CA INDEX NAME)



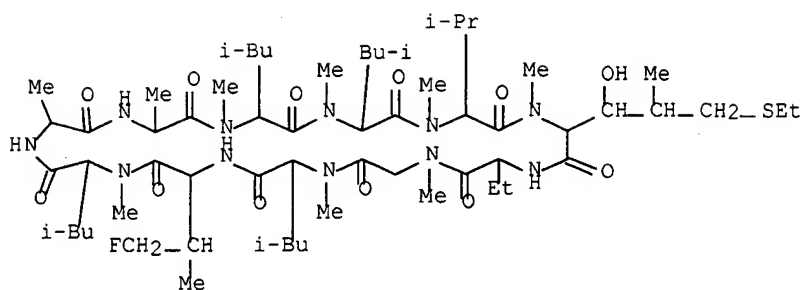
RN 130840-76-5 HCAPLUS

CN Cyclosporin A, 6-[(3R,4S)-3-hydroxy-N-methyl-5-(methylthio)-L-leucine]-10-(4-fluoro-L-valine)- (9CI) (CA INDEX NAME)



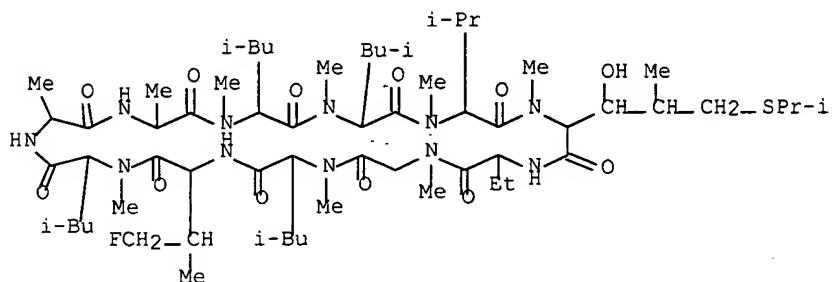
RN 130840-77-6 HCAPLUS

CN Cyclosporin A, 6-[(3R,4S)-5-(ethylthio)-3-hydroxy-N-methyl-L-leucine]-10-(4-fluoro-L-valine)- (9CI) (CA INDEX NAME)



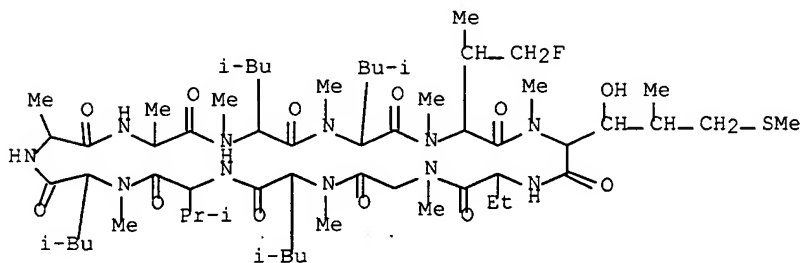
RN 130840-78-7 HCAPLUS

CN Cyclosporin A, 6-[(3R,4S)-3-hydroxy-N-methyl-5-[(1-methylethyl)thio]-L-leucine]-10-(4-fluoro-L-valine)- (9CI) (CA INDEX NAME)



RN 130840-79-8 HCAPLUS

CN Cyclosporin A, 5-(4-fluoro-N-methyl-L-valine)-6-[(3R,4S)-3-hydroxy-N-methyl-5-(methylthio)-L-leucine]- (9CI) (CA INDEX NAME)



RN 130840-80-1 HCAPLUS

CN Cyclosporin A, 5-(4-fluoro-N-methyl-L-valine)-6-[(3R,4S)-5-(ethylthio)-3-hydroxy-N-methyl-L-leucine]- (9CI) (CA INDEX NAME)

